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Toward precision smoking cessation treatment I: Moderator results from a factorial experiment

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ABSTRACT

Background: The development of tobacco use treatments that are effective for *all* smokers is critical to improving clinical and public health. The Multiphase Optimization Strategy (MOST) uses highly efficient factorial experiments to evaluate multiple intervention components for possible inclusion in an optimized tobacco use treatment. Factorial experiments permit analyses of the influence of patient characteristics on main and interaction effects of multiple, relatively discrete, intervention components. This study examined whether person-factor and smoking characteristics moderated the main or interactive effects of intervention components on 26-week self-reported abstinence rates.
Methods: This fractional factorial experiment evaluated six smoking cessation intervention components among primary care patients (N = 637): Prequit Nicotine Patch vs. None, Prequit Nicotine Gum vs. None, Preparation Counseling vs. None, Intensive Cessation In-Person Counseling vs. Minimal, Intensive Cessation Telephone Counseling vs. Minimal, and 16 vs. 8 Weeks of Combination Nicotine Replacement Therapy (NRT; nicotine patch + nicotine gum).
Results: Both psychiatric history and smoking heaviness moderated intervention component effects. In comparison with participants with no self-reported history of a psychiatric disorder, those with a positive history showed better response to 16- vs. 8-weeks of combination NRT, but a poorer response to counseling interventions. Also, in contrast to light smokers, heavier smokers showed a poorer response to counseling interventions.
Conclusions: Heavy smokers and those with psychiatric histories demonstrated a differential response to intervention components. This research illustrates the use of factorial designs to examine the interactions between person characteristics and relatively discrete intervention components. Future research is needed to replicate these findings.

1. Introduction

Tobacco smoking remains the leading preventable cause of mortality and morbidity in developed countries, underscoring the continued need for highly efficacious smoking treatments (U.S. Department of Health and Human Services, 2014). Even with the best smoking cessation treatments that comprise both counseling and pharmacotherapy, about two-thirds of smokers fail to achieve long-term abstinence (Fiore et al., 2008; West et al., 2015). Smoking rates remain especially high amongst certain groups of smokers, such as those with psychiatric comorbidity and those with lower educational attainment (Centers for Disease Control and Prevention, 2013; Jamal et al., 2014). Therefore, it is of considerable public health importance that such populations benefit from

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smoking cessation treatments. Further, it is important to determine whether person factors (e.g., gender, race) or smoking-related factors (e.g., tobacco dependence) might effectively guide treatment selection or allocation (Hughes, 2013; Loh et al., 2012).

Most prior attempts to evaluate the moderation of treatment response have been obscured by the use of randomized controlled trials (RCTs) that evaluated only groups of components (e.g., pharmacotherapy + various counseling elements) and did not manipulate discrete intervention components. The Multiphase Optimization Strategy (MOST) has been proposed as an efficient way to engineer more effective treatment packages by using screening experiments to identify especially effective intervention components which can be combined into a treatment package and ultimately evaluated in a traditional RCT (Collins et al., 2016, 2005). Screening experiments frequently use factorial designs, which allow researchers to identify the main and interactive effects of the evaluated intervention components (Collins et al., 2016, 2005). Factorial designs can also reveal how person factors moderate the effects of individual intervention components, or combinations of components. In other words, factorial designs can provide insight into how individuals' characteristics predict differential response to multiple, discrete intervention components or to combinations of components. Identifying differential response to interventions by different types of smokers could be used to personalize treatment and provide insight into factors that influence intervention effectiveness. Conversely, a lack of interactions between intervention components and person factors would support the robustness and stability of treatment effects.

A recent smoking cessation screening fractional factorial experiment (Piper et al., 2016) evaluated the main and interactive effects of six intervention components selected to address the challenges smokers face during different phases of smoking treatment (Baker et al., 2011). This screening study is part of a program of research using MOST (Piper et al., 2016) to engineer an optimized smoking cessation treatment. There were no significant main effects on long-term (26 week) point-prevalence abstinence, but there were three significant two-way interactions. As an important step in the MOST approach to treatment development, the goal of this research was to explore the stability of the effects of multiple, relatively discrete intervention components. Despite the absence of main effects, some of the intervention components might be meaningfully effective in some subgroups of participants and this could guide the development of treatment algorithms. Examining moderation effects might also shed light on the unexpected finding of significant interaction effects amongst intervention components. Such moderation effects could also have theoretical value; they could provide information about individual risk factors (e.g., high tobacco dependence) that are especially addressed by different intervention components. Therefore, this research sought to determine whether easily assessable person factors (e.g., gender, race, education, psychiatric history) and smoking-related variables (e.g., dependence, smoking rate, living with a smoker) moderated the individual and joint effects of six smoking cessation intervention components.

2. Methods

2.1. Procedure

This is a secondary data analysis of a fractional factorial screening experiment that assessed the effects of six smoking cessation intervention components on long-term abstinence (see Piper et al., 2016 for additional details including the CONSORT diagram). A total of 637 participants were recruited during primary care clinic visits and screened for eligibility: ≥18 years old; ≥5 cigarettes/day for the previous 6 months; motivated to quit; not currently taking bupropion or varenicline; agreeing to use only study medication for the duration of the study; no medical contraindications to NRT; no self-reported history of psychosis or bipolar disorder; and, for women of childbearing potential, agreeing to use an approved method of birth control during treatment. Eligible participants provided written informed consent, completed initial assessments, and received their interventions at their primary care clinic. A research database created intervention and assessment schedules, based on randomly assigned treatment conditions, which guided delivery of the interventions by bachelor's level case managers supervised by licensed clinical psychologists.

2.2. Experimental design

This experiment used a balanced fractional factorial design with six factors: 1) Prequit Nicotine Patch vs. None; 2) Prequit Nicotine Gum vs. None; 3) Preparation Counseling vs. None; 4) Intensive Cessation In-Person Counseling vs. Minimal; 5) Intensive Cessation Phone Counseling vs. Minimal; and 6) 16 vs. 8 Weeks of Combination NRT. These factors were chosen to address specific challenges that emerge early in the quit attempt, based on theory and extant research (Baker et al., 2011), and to be easily translated into real-world healthcare settings (Piper et al., 2016). The Resolution VI fractional factorial design reduced the number of conditions from 64 to 32 and allowed for the estimation of main effects and two-way interactions only (Collins et al., 2016; Piper et al., 2016). Randomization was stratified by gender and clinic. Staff were blinded to randomization until eligibility was confirmed; participants were blinded until consent was provided.

2.3. Experimental factors

2.3.1. Prequit nicotine patch. Half the participants were assigned to the active condition and received 14-mg patches for the 3 weeks prior to the target quit day (TQD) while the other half did not receive prequit patches.

2.3.2. Prequit nicotine gum. Participants in the active condition received 2-mg nicotine gum for the 3 weeks prior to the TQD (≥9 pieces of gum/day, 1 piece/1–2 h); the other half did not. Participants who received both Prequit Patch and Gum were told to use at least 5 pieces/day of gum, unless such use produced adverse effects.

2.3.3. Preparation counseling. Participants in the active condition received three 20-min counseling sessions prior to the TQD, focused on coping skills, reduction, and making practice quit attempts, while the other half of participants did not. The sessions 3 weeks and 1 week before the TQD (Weeks -3 and -1) were in-person, and the Week -2 session was over the phone.

2.3.4. In-person counseling. Participants in the intensive condition received three 20-min face-to-face counseling sessions: one week pre-TQD, on the TQD, and at Week 1. Sessions focused on skill building and intra-treatment social support. Participants assigned to the minimal level received one 3-min in-person session at Week -1.

2.3.5. Phone counseling. Participants in the intensive condition received three 15-min phone sessions (TQD, Days 2 and 10), focused on coping skills, avoiding smoking cues, and intra-treatment social support. Participants assigned to the minimal condition received one 10-min session on the TQD. Thus, all participants received some TQD phone counseling.

2.3.6. Extended medication. All participants received combination NRT (nicotine patch + nicotine gum) starting on their TQD. Half